MOLECULAR

Section I - DNA Replication

I. DNA structure (Figure 2.1.1)

- A. DNA is complementary to the opposite strand (cytosine pairs with guanine and thymine pairs with adenine).
- B. DNA wrapped around eight histones is called a nucleosome.
- C. The first histone (H_1) is responsible for linking nucleosomes together.
- D. Nucleosomes tightly packed together results in the formation of a chromosome.
  1. Tightly packed → heterochromatin (not accessible to transcription proteins)
  2. Loosely packed → euchromatin (transcriptionally active)
- E. Histone methylation → ↓ DNA transcription
- F. Histone acetylation → ↑ DNA transcription

II. DNA replication (Figure 2.1.2)

- **A.** Helicase separates the DNA at the replication fork.
- B. Single-stranded binding proteins bind to the DNA and prevent the two strands from reannealing.
- C. The region where DNA replication begins is called the origin of replication.
- D. Primase anneals to the 3' end of the DNA and synthesizes a primer.

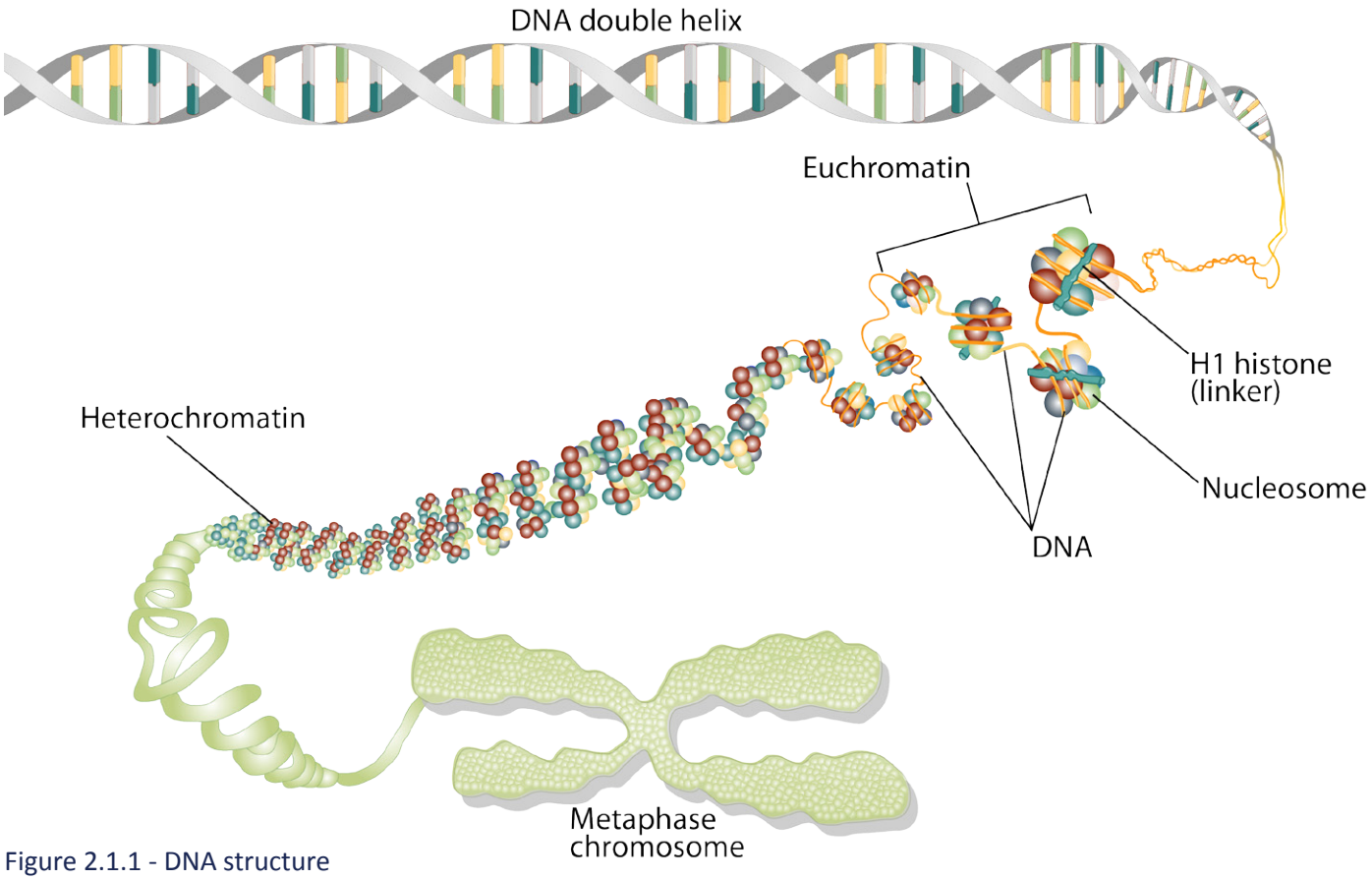


Figure 2.1.1 - DNA structure

E. DNA polymerase III binds to the primer and adds deoxynucleotides onto the 3' end of the primer (eukaryotes perform this function via DNA polymerase epsilon).
   1. Synthesizes DNA in the 5' → 3' direction.
   2. 3' → 5' exonuclease activity.

F. The DNA strand being synthesized towards the replication fork is called the leading strand.
   1. Synthesized continuously

G. The DNA strand being synthesized away from the replication fork is called the lagging strand.
   1. Synthesized discontinuously resulting in the formation of Okazaki fragments.

H. DNA polymerase I (eukaryotes perform removal of primers via DNA polymerase delta) removes the RNA primers and replaces them with DNA.
   1. Synthesizes DNA in the 5' → 3' direction.
   2. 5' → 3' exonuclease activity.

I. DNA ligase joins the Okazaki fragments

J. Topoisomerases remove supercoils in DNA.
   1. Prokaryotic (topoisomerase II & IV)
      a) Fluoroquinolones
   2. Eukaryotic (topoisomerase I & II)
      a) Irinotecan
      b) Topotecan
      c) Etoposide
      d) Teniposide

K. DNA polymerase I vs DNA polymerase III
   1. DNA polymerase I ("DNA polymerase I only goes in one direction")
      a) 5' → 3' synthesis ("contrive at five")
      b) 5' → 3' exonuclease

L. DNA polymerase III
   1. 5' → 3' synthesis
   2. 3' → 5' exonuclease

M. Telomerase
   1. Telomere: region at the end of a chromosome
   2. Telomerase: enzyme that adds DNA to the 3' end of chromosomes to prevent the loss of genetic material with every duplication.

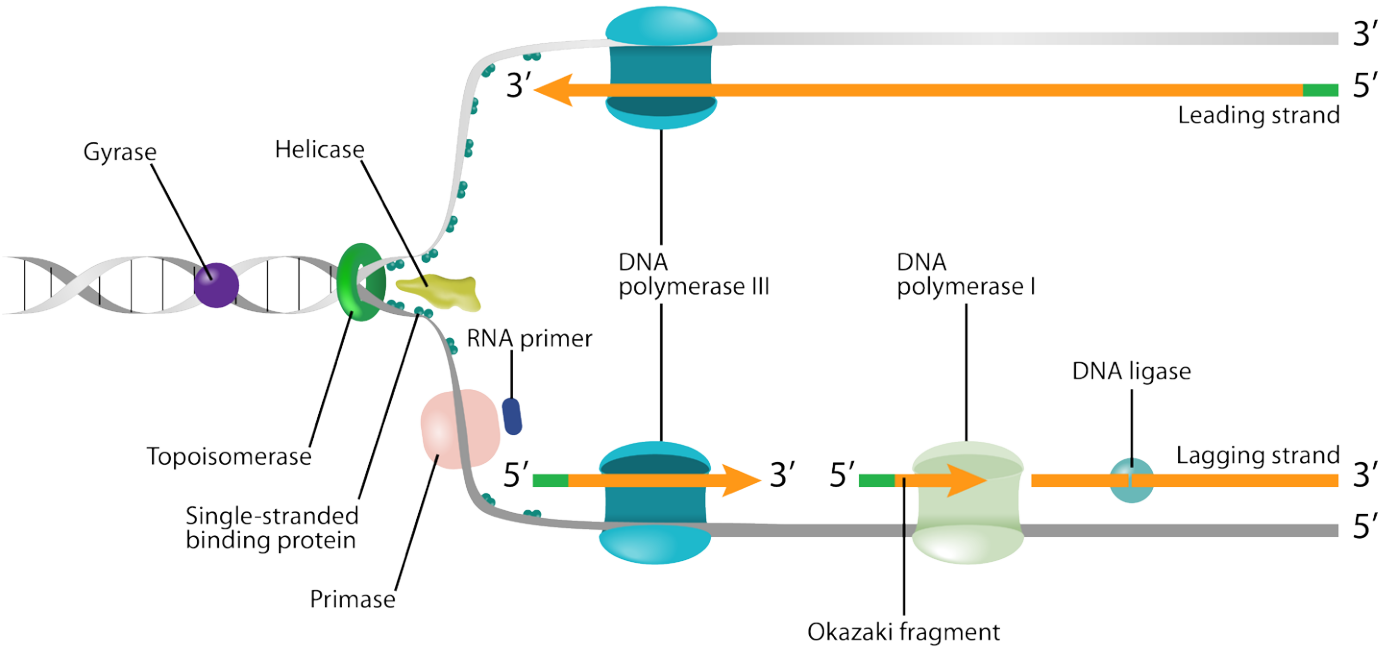
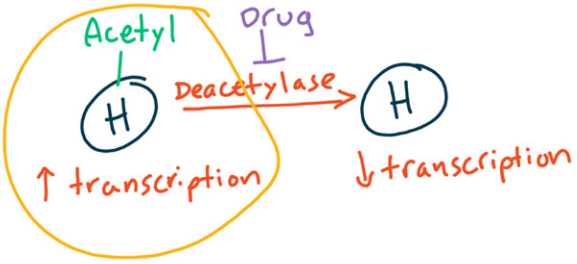


Figure 2.1.2 - DNA replication

REVIEW QUESTIONS

1. A new experimental drug is found to inhibit histone deacetylase. How will this drug most likely alter transcription?

   - **Acetylation of histones → ↑ transcription**
   - **Deacetylation of histones → ↓ transcription**
   - **Deacetylase is an enzyme that removes acetyl groups on histones**
   - **The drug described inhibits deacetylase → ↑ number of acetylated histones → ↑ transcription**



2. A pathologist is studying DNA from staph aureus wound infections. She isolates an enzyme and studies its activity during DNA replication. She finds that this particular enzyme possesses 5' to 3' exonuclease activity. What enzyme has she most likely isolated?

   - **DNA polymerase I has 5' to 3' exonuclease activity**

3. A 76-year-old male is admitted to the hospital for community acquired pneumonia. A sputum culture is obtained in hopes of isolating the pathogen and determining antibiotic sensitivity. As the organism grows, its DNA is extracted and analyzed. Detailed analysis of fragments from partially replicated DNA reveals the presence of ribose sugar molecules with an increased number of hydroxyl modifications. These fragments are most likely degraded by what enzyme during DNA replication?

   - **"Detailed analysis of fragments from partially replicated DNA reveals the presence of ribose sugar molecules with an increased number of hydroxyl modifications." → referencing RNA (ribose contains one more hydroxyl group than deoxyribose)**
   - **During DNA replication RNA is present in the form of primers**
   - **RNA primers are degraded by the enzyme DNA polymerase I**